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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/464,303	12/15/1999	GREGORY L. STAHL	B0801/7156	7348

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HELEN C LOCKHART
WOLF GREENFIELD & SACKS P C
600 ATLANTIC AVENUE
BOSTON, MA 02210

EXAMINER	
DECLOUX, AMY M	
ART UNIT	PAPER NUMBER
1644	13

DATE MAILED: 05/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/464,303	Applicant(s) STAHL ET AL.	
	Examiner Amy M. DeCloux	Art Unit 1644	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34 and 36-41* is/are pending in the application.

4a) Of the above claim(s) *1-17 and 36-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment filed 2-11-2002 (Paper No. 11) is acknowledged and has been entered. Applicant's supplemental IDS filed 3-25 (Paper No. 12) is acknowledged and has been considered.

2. The outstanding rejections and objections can be found in the previous office action, mailed 7-31-01 (Paper No. 9). In view of applicant's amendment, declaration and arguments filed 2-11-02, the outstanding 112 rejections have been withdrawn. However, a new grounds of rejection has been applied to the newly amended claims.

3. Claims 19-21, 23-25 and 28-32 have been accorded the filing date (12-15-1998) of the claimed priority document US 60/112,390, in light of applicant's comments.

4. Formal drawings and/or photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the PTO-948 form attached to the office action mailed 7-31-01 (Paper No. 9).

A). Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for

filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B) Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDONMENT of the application.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 18-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. This is a new matter rejection .

Claims 18-34 are not supported by the specification or by the claims as originally filed. There is no support in the specification or claims as originally filed for the recitation of a composition comprising an MBL inhibitor wherein the isolated MBL binding peptide has an MBL binding $CDR3_1$ region or a functional variant thereof of a monoclonal antibody produced from a hybridoma cell line $_{(2A9)}$. There is no written description of the claimed invention in the specification or claims as originally filed. Thus the claimed invention constitutes **new matter.**

7. Claims 18-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 18-34 encompass a composition comprising an MBL inhibitor comprising a peptide comprising an MBL CDR3 region of three recited antibodies, or a functional derivative thereof, which applicant has described on page 19, lines 25-30 of the instant specification as having the sequence of said CDR3 regions with conservative substitutions therein.

The instant disclosure of three antibodies that bind MBL and inhibit LCP associated complement activation does not adequately describe the scope of the claimed genus any MBL inhibitor that has one of the three recited CDR3 regions or a functional variant thereof, each of which encompasses a substantial variety of subgenera. Since the MBP binding peptide, comprises a CDR3 region or functional variant thereof, said peptide can also encompass an indeterminate number and type of additional amino acids, in addition to the recited CDR3 region or variant thereof. Further, with regard to a functional variant of the recited CDR3 regions, any number and combination of amino acids can be substituted in said CDR3 region. Since an indefinite number and type of additional amino acids may also be encompassed by the recited peptide, the composition of the instant claims is not adequately described, especially given that the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify a peptide encompassed by the method recited in the instant claims. Therefore, the structure of "an isolated MBL binding peptide " is not conventional in the art and one of skill in the art would not recognize from the disclosure that applicant was in possession of the of "an isolated MBL binding peptide " encompassed by the method of the claimed invention.

It is noted that though the claimed invention is directed to polypeptides and not cDNA, the principle of the following still holds for said polypeptides: a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a

recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly&Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

8. Claims 18-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising an MBL inhibitor comprising an antibody produced by the hybridoma cell lines 2A9, 3F8 and hMBL1.2, does not reasonably provide enablement for the broader recitation of a composition comprising an MBL inhibitor comprising any peptide comprising an MBL CDR3 region of said antibodies, or any functional derivative thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed in the instant claims without an undue amount of experimentation. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims.

The instant specification provides enablement only for a composition comprising an MBL inhibitor comprising an antibody produced by the hybridoma cell lines 2A9, 3F8 and hMBL1.2 . However the specification fails to provide guidance as to how to make or use a composition comprising any other MBL binding peptide, as recited in the instant claims. Because Janeway et al. (Immunobiology 4rth Edition, (1999), page87) teaches that antibody specificity of an antibody is determined by the

CDR1, CDR2 and CDR3 regions of the heavy and light chains, one of skill would require more guidance and direction from the instant specification regarding the effectiveness of any peptide comprising one of the recited CDR3 regions in binding MBL and inhibits LCP associated complement activation.

The instant specification defines "functional variant" as a peptide having the sequence of said CDR3 regions with conservative substitutions therein (see page 19, lins 25-30). Accordingly, the specification fails to provide guidance as to how to make or use a composition comprising a functional variant of said MBL binding peptide, essentially for the reasons described supra.

Predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functions and properties requires a knowledge of, and guidance with regard to which amino acids in the sequence, if any, are tolerant of modification and which are conserved or less tolerant to modification, and detailed knowledge of the ways in which the product's structure relates to its functional usefulness, as evidenced by the teachings of Abaza et al (J. Of Protein Chemistry, 11(5):433-444, 1992). Abaza et al teach that even a single amino acid difference in an antigen may effect antibody binding by teaching that an amino acid substitution of myoglobin outside the epitope recognized by a monoclonal antibody causes the myoglobin to be unreactive with said antibody, (see entire article, especially the Abstract). Therefore, predicting which polypeptides comprising the recited CDR3 regions and/or variants thereof, will retain the recited ability to inhibit LCP associated complement activation is complex and well outside the realm of routine

experimentation. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Furthermore, the specification fails to provide guidance as to how to make or use a polypeptide that comprises the recited CDR3 regions or variants thereof. By reciting the term "comprises" in the instant claims, said polypeptide can also encompass an indeterminate number and type of additional amino acids, in addition to the amino acids in the recited SEQ ID NO:s. Given the indefiniteness of the additional amino acids that may be encompassed in the polypeptide of the instant claims, and given that the unpredictability of which changes (including additions) can be tolerated in a polypeptide's amino acid sequence and still retain similar functions and properties requires a knowledge of, and guidance with regard to which amino acids, if any, can be added, and detailed knowledge of the ways in which the product's structure relates to its functional usefulness, especially in view of the teachings of Abaza et al (see supra).

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute.

9. No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. This application contains claims 1-17 and 36-41 drawn to an invention nonelected with traverse in Paper No. 8, filed 4-23-01. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy M. DeCloux whose telephone number is 703 306-5821. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703 308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703 305-3014 for regular communications and 703 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

Amy DeCloux, PhD
Patent Examiner, 1644
May 4, 2002

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644